Somatosensory evoked fields in acute stroke

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1 Introduction

Stroke is probably the commonest cause of chronic and severe disability in the western countries and accounts for a large proportion of healthcare resources. In the last decades the rate of mortality has progressively decreased, shifting the focus of research and health organizations on the analysis of mechanisms for functional recovery and rehabilitation. The capabilities of neurones, neural circuits and complex brain structures to recovery after injury are not completely understood. Long-lasting changes in neural circuits and in brain connectivity following a cerebral lesion demonstrated in animal models, are, at least in part, the biological basis of recovery from injury. Within this frame, modern techniques aiming to investigate brain function are playing a progressively more important role.

A roughly symmetrical organization of sensorimotor areas in right and left hemispheres has been found in healthy humans by different methods of functional brain imaging, including Positron Emission Tomography (PET), fMRI and magneto-encephalography (MEG) [1,2]. Post-lesion neural reorganization -when occurring in the middle cerebral artery territory following a monohemispheric stroke- might significantly modify the interhemispheric symmetry of the sensorimotor cortices somatotopy. MEG allows to non-invasively identify cortical generators, which can be precisely allocated within the individual brain 'anatomy' by integrating MEG findings with CT or MR brain images [3,4]. Moreover, the presence of lesioned tissue near the generator source scarcely affects the scalp distribution of the magnetic fields. MEG has been used in stroke patients in a stabilized condition showing a high percentage of somatotopical reorganization in the affected hemisphere [5,6]. Recently, absolute spatial and strength parameters of ECD, in the affected hemisphere were studied in early stages of stroke patients [7]; however, in this study no emphasis was put on essential interhemispheric differences of the examined parameters. In the present study, we evaluated acute stroke patients by using MEG within 10 days after symptom onset. The aim of the present study was to investigate how the sensory processing and the organization of the cortical areas change in patients with infarctions of the middle cerebral artery (MCA) territory including sensorimotor cortex or its underlying white matter. The MEG data were correlated with the clinical data, as assessed by the NIH stroke scale score (NIHSSS) and the evaluation of independence in activities of daily living (Barthel Index), and a motor and sensory score for the upper limb.

2 Methods

2.1 Patients

Eighteen patients with a mean age of 68±9 years (7 females) admitted to our hospital with first acute ischemic stroke involving the MCA were enrolled in the study. Patients were excluded if they had neuroradiological evidences of cerebral atrophy or multifocal hypoxic-ischemic encephalophaties, peripheral neuropathies (making sensory testing and nerves stimulation unsuitable), and dementia (making patients uncooperative). The local Ethical Committee approved the experimental protocol and a written informed consent was obtained by all patients. The NIH stroke scale \score (NIHSSS), the evaluation of independence in activities of daily living (Barthel Index), a hand motor score and a detailed sensory test was used for neurological assessment of the stroke severity.

2.2 MEG investigation

Somatosensory Evoked Fields (SEFs) were recorded following separate electrical stimulation of left and right median nerves at wrist, inside a magnetically shielded room. A 28-channel system [1] covering a total scalp area of about 180 cm^2 was used, and data were collected from the contralateral hemisphere only, accordingly to the SEF analysis, focusing on the two initial deflections (M20, M30): these components are the most stable and repeatable, independent from the subject attention and selectively generated in the sensorimotor areas contralateral to the stimulated hand. Equivalent Current Dipole (ECD) characteristics (spatial coordinates and strength) were calculated at 1 ms intervals in the 15-50 ms post-stimulus epoch, using a moving dipole model inside an homogeneously conducting sphere. The localization results were accepted only if their explained variance was above 90% (therefore, the influence of other adjunctive dipoles was less than 10%) and were expressed in a coordinate system defined on the basis of individual anatomical landmarks. Data in patients were evaluated on the basis of a normative data set, constructed via the localization results in 20 healthy subjects. Normative data included absolute spatial parameters as well as the limits of interhemispheric difference [1]. This method allowed to predict the region in each hemisphere where the examined ECD was expected to fall in, by knowing the location in the contralateral one after stimulation of the opposite hand. Normative limits were calculated also for absolute and asymmetry of latencies, strengths and the extension of the cortical region deserved to the contralateral hand representation.

A waveshape analysis was carried out via a correlation method comparing the SEF morphology in the two hemispheres [8]. The channels with SEFs of maximal amplitude in each hemisphere were selected and the waveform correlation was calculated in two succeeding time intervals starting from the M20 onset, to focus waveform comparative analysis only to the epoch following the arrival of sensory input to the post-central cortex (wave M20, known to be the marker of the somatosensory inflow arrival to primary sensory cortex). The first interval lasted 30 ms and the following starting at the end of this one lasted 50 ms; two parameters evaluated the wave shape intehemispheric similarity in primary sensorimotor areas (interhemispheric correlation = IHC_SI, [8]), and in parietal ones (IHC_par). For these parameters too normative limits were calculated to detect eventual activation pattern alteration in the affected hemisphere of patients.

2.3a MRI investigation for lesion study

Brain MRI were performed with a permanent magnet operating at 1.5 T. T1 and T2 weighted images were obtained and T1 weighted images were also obtained after intravenous administration of gadolinium DTPA, providing ischemic lesion images in sagittal and axial planes.

2.3b MRI investigation for ECD localization

Brain MRI were performed with a permanent magnet operating at 1.5 T. A Spin-Echo T1 weighted sequence (500/25) was used, providing contiguous 5 mm thickness slices in sagittal and axial planes. The MEG-MRI common reference system was defined on the basis of three landmarks fixed on nasion, left and right pre-auricular points. The MRI scan planes were set parallel to the above-defined localization coordinate system. In this way, superimposition on MR images achieves a precision of 2-3 mm [9]. Following a standard brain atlas, MEG locations of the patients were integrated with individual MR images.

3 Results

3.1 Clinical and radiological findings

All the patients presented different degrees of hemiparesis mainly involving the upper limb and 11 of 18 patients showed different degrees of hypoesthesia of the affected side. Clinical data are reported in the table. In all cases, MRI was performed a few days after the MEG session. Frontal lobe was involved in 5 patients, parietal lobe was involved in 11 patients, internal capsule was involved in 4 patients, while thalamus and basal ganglia were involved in 5 and 3 cases, respectively.

3.2 MEG analysis

In 15 patients, both the M20 and M30 components were reliably identified. In three patients, the entire SEFs were missing on the affected hemisphere. MEG data are reported in the table.

Subj	**Gender**	**Age**	**side**	**NIH**	**BI**	**IHC_SI**	**IHC_PAR**	**loc_asy (20)**	**loc_asy (30)**	**time_asy (20)**	**time_asy (30)**	**s_asy (20)**	**s_asy (30)**
1	m	63	r	5	100	**0,85**	0,97						
2	f	75	r	6	70	**0,79**	0,78	+	+			<	
3	m	64	l	3	100	**0,58**	**0,30**		+				
4	m	66	r	5	75	**0,01**	**0,56**		+	+	+		>
5	m	52	l	6	80	**0,70**	**0,08**	+		+			
6	m	58	l	2	100	0,99	0,97						>
7	f	75	r	4	80	**0,03**	**0,13**						
8	m	75	r	14	40	**0,26**	**0,39**					a	a
9	f	72	r	14	60	**0,02**	**0,62**			+			
10	m	72	r	6	90	**0,19**	**0,48**			+		<	<
11	m	76	l	6	60	**0,46**	0,92					a	a
12	m	70	l	11	70	**0,23**	**0,53**	+	+		+	<	>
13	f	86	r	4	100	0,98	0,99					<	
14	f	57	r	9	70	**0,07**	**0,40**					a	a
15	m	67	r	7	70	**0,91**	0,83						>
16	m	65	l	5	60	0,99	0,93				+		
17	f	76	l	7	70	**0,78**	**0,60**						
18	m	58	l	4	100	**0,48**	0,86				+		

Latencies: M20 and M30 peak latencies were always normal on the unaffected hemisphere; on the other hand, latencies were significantly prolonged on the affected hemisphere in 7 of 15 patients (46.6%, excluding the three patients, with no SEF recognizable in the affected hemisphere). Latency delays similarly, but often independently, affected the M20 and M30 components. When analyzing ECD latencies with respect to the clinical scores, the mean number of delayed ECDs was slightly, but not significantly, larger in patients with higher NIHSSS score (7.3± 3.8 vs 5± 2.2).

Strengths: Among the 15 patients with recognizable SEF on the affected hemisphere, 4 showed strength asymmetries between the two hemispheres for the M20 ECD, and 5 for the M30: the M20 ECD resulted always reduced in the affected hemisphere, whereas M30 was amplified in the AH in 4 out of 5 cases (Fig 1).

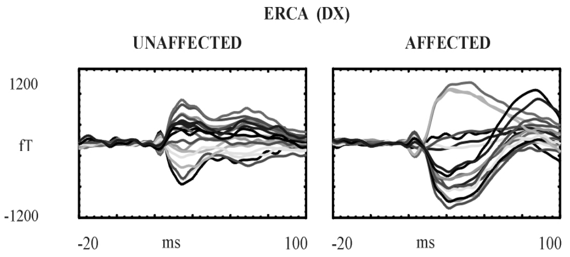

Figure 1: *Patient 15 (67 y.o.; cortical ischaemic stroke, lesion in right sensory cortex).SEF recordings from the UH and from the AH in the acute phase of stroke showing the waveshape asymmetry and amplification of M30 and parietal components of SEF after median nerve stimulation on the AH.*

ECD Locations: in the affected hemisphere: after exclusion of the 3 cases with missing SEFs, 5 out of the remaining 15 cases showed SEF abnormalities for the location of the ECD. All ECDs were localized well outside the area of structural lesion as evaluated by MEG/MRI integration. In relation with the clinical scores, the altered ECD locations did not correlate with the NIHSSS score (6.2± 3 vs 5.8± 3).

Morphology: The waveshape analysis showed a significant asymmetry in 53% of measurable cases (8 patients out of 15, SEF being not recordable from affected hemisphere in three patients). When analyzing waveshape with respect to the clinical scores including in the analysis also the three patients without a recognizable SEF on the affected hemisphere, the number of asymmetric waveshape was slightly larger in patients with higher NIHSSS score (7.5± 3.8 vs 5.1± 1.8).

4 Discussion

The estimation of sensory impairment is important because subtle sensory disturbances might be related to clinical outcome [10]. In fact, if somatosensory feedback is disturbed, the functional motor deficit recovers to a lesser degree (i.e., in those thalamic lesions extending into the posterior limb of the internal capsule). Such a role of thalamic afferents to sensorimotor brain areas, as well as of postcentral parietal structures in the mechanism of motor recovery, is emphasized by PET studies both in animal models and in humans [11,12,13].

In humans, motor and sensory cortices partly overlap and are not simply separated by the central sulcus; they greatly vary in their extension and with respect to the central sulcus [14]. Matching MEG results with the clinical score, our data showed that the ECDs were more altered in strength and waveshape asymmetry in patients with worst clinical picture. These alterations in ECD parameters possibly may help to quantitatively assess the cortical damage of the hand sensory area following both a cortical and/or a subcortical ischemic unilateral lesion.

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